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10/539,093	06/15/2005	John M. Yanni	2394 US F	9226

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Alcon Research
6201 South Freeway
Fort Worth, TX 76134-2099

EXAMINER	
SINGH, ANOOP KUMAR	
ART UNIT	PAPER NUMBER
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,093	YANNI ET AL.	
	Examiner	Art Unit	
	Anoop Singh	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-22 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-22 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 12/13/05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-22 are under consideration.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited on PTO-1449 or by the examiner on form PTO-892, they have not been considered.

The information disclosure statement (IDS) submitted on 12/13/2005 has been considered by the examiner.

Specification

The amendment filed 12/5/2005 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. In the instant case, the sequence listing filed on 12/5/2005 is not supported by original disclosure.

Applicant is required to cancel the new matter in the reply to this Office Action.

New Matter-Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 9-13, 14-15 and 18-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

37 CFR 1.118(a) states "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". In the instant case, the recitation of limitation "SEQ ID NO: 1-4" (claims 1, 4, 5, 6, 14, 15) is considered new matter. Applicants do not have support of specific sequence ID No at the time of filing of the specification. Upon further review of the instant specification, examiner could only find references made to SEQ ID NO: 1-4 while describing the invention without providing the actual sequences at the time of filing of instant specification. Thus, the specific sequences set forth in SEQ ID NO: 1, 2, 3, and 4 as recited in claims 1, 4, 5, 6, 14, 15 do not have any explicit support in the specification.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph-written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981) teaches that "Whenever

the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time application was filed...If a claim is amended to include subject matter, limitation or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application".

To the extent the claimed invention embrace delivering a composition comprising SEQ ID NO: 1-4 that is not described in the instant disclosure. Claims 1-6, 9-13, 14-15 and 18-22 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It is noted that Applicants original disclosure do not teach the sequence comprising Seq ID NO: 1-4 that is delivered to the eye for the treatment of dry eye condition. As described before, the specification does not provide adequate guidance on determining the specific sequence of SEQ ID NO: 1-4 as embraced by the claims and therefore an artisan of skill would require undue experimentation to practice or make and/or use the invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In determining whether Applicant's claims are enabled, it must be found that one of skill in the art at the time of invention by applicant would not have had to perform "undue experimentation" to make and/or use the invention claimed. Such a determination is not a simple factual consideration, but is a conclusion reached by weighing at least eight factors as set forth in In re Wands, 858 F.2d at 737, 8 USPQ 1400, 2d at 1404. Such factors are: (1) The breadth of the claims; (2) The nature of the invention; (3) The state of the art; (4) The level of one of ordinary skill in the art; (5) The level of predictability in the art; (6) The amount of direction and guidance provided by Applicant; (7) The existence of working examples; and (8) The quantity of experimentation needed to make and/or use the invention.

The office has analyzed the specification in direct accordance to the factors outlines in *In re Wands*. MPEP 2164.04 states: "[W]hile the analysis and conclusion of a lack of enablement are based on factors discussed in MPEP 2164.01(a) and the evidence as whole, it is not necessary to discuss each factor in written enablement rejection." These factors will be analyzed, in turn, to demonstrate that one of ordinary

skill in the art would have had to perform "undue experimentation" to make and/or use the invention and therefore, applicant's claims are not enabled.

Claim 1 embraces a method for treating dry eye by obtaining the composition comprising SEQ ID NO: 1 or 3 and administering the composition to any patient suffering from dry eye such that therapeutic gene product is expressed. The dependent claims 2-3 limits the method to include composition containing a vector comprising a nucleic acid encoding the gene product that is administered either topically or by using ocular drops or an ointment. It is noted that while claim 4 is directed to a composition comprising a vector comprising sequence set forth in SEQ ID NO: 1 or 3 and pharmaceutical excipient, these compositions have been analyzed for their intended use in the treatment in dry eye condition. Claims 5-8, 14-17 are directed to a method for treating dry eye condition by increasing the level of a therapeutic gene product in a postmenopausal patient by incorporating nucleic acid expression in ocular cell such that nucleic acid is expressed and patient is treated. Subsequent claims further limit the cells to include conjunctiva or corneal epithelial cells that is debrided under conditions permissive for the uptake of nucleic acid. Claims 9-13 and 18-22 limit the nucleic acid to include viral vector, plasmid for delivering the gene to be expressed in ocular cells. The subsequent claims limit nucleic acid to include retro or adeno or adeno-associated viral vector.

The aspects considered broad are the breadth of any subject population subsequently limiting to postmenopausal patient, using any method or vector that could be used for treating dry eye condition subsequently limiting to few, any method of

administration to affect eye subsequently limiting to drops or ointment, the increase of expression of transgene in many ocular cells then limiting to conjunctival or corneal epithelial cell and transgene not operably linked to expression control elements a critical limitation not described in claims.

The claims 1-8 and 15-17 are directed to increasing the levels 15-lipoxygenase-1 (15-LO-1) or 15-lipoxyngenase-2 (15-LO-2) transgene expression in eye of any subject subsequently limiting to postmenopausal patient administered via any route subsequently limiting to topical application such that dry eye condition is treated. Additionally, the invention embraces treating dry eye condition of postmenopausal patient that is interpreted to have use in the art for treating postmenopausal women.

The nature of such invention is within the broad genera of gene therapy, and gene therapy is not generally enabling of Applicant's invention due to problems with, *inter alia*, targeting and expression of transgenes at therapeutically effective level by administering composition via any route and method in any specific tissue. For purposes to be shown in the state of the prior art, the question of lack of enablement is discussed.

The specification broadly discloses the need for composition and treatment for dry eye condition particularly in postmenopausal women (pp. 2). The invention is based in part on the discovery that mucin reside in the apical and sub apical corneal epithelium which is secreted via cornea apical, sub apical cells and conjunctival epithelium of human eye (pp 3-4). Page-5 describes different part of the body that produces and secretes mucin and it briefly lists agents that increase mucin and/or tear production.

Page-5 broadly tracks claim language. The present inventor discloses that ocular surface epithelium of postmenopausal women lack 15-lipoxygenase. This is required for the synthesis of 15(s)-HETE, which in turn stimulates the production of MUC-1 mucin (pp 6). Pages 7-12 broadly discuss role of lipoxygenase, *in situ* ocular cells, method and type of vector and its use, target ocular cells and permissive condition of nucleic acid uptake for the treatment of dry eye condition.

However, such broad disclosure does not demonstrate the information required by the Artisan to reasonably predict that any transgene can be expressed in ocular cells of any subject or human at minimum effective levels for therapeutic response. The specification does not provide any specific guidance for expressing the nucleic acid Seq ID no 1 or 3 at therapeutic effective level in ocular cells of postmenopausal women.

In fact, the art of gene therapy at the time of the filing of this application was unpredictable since numerous factors complicate the gene delivery art that is difficult to be overcome by routine experimentation. These include, the fate of DNA vector itself, volume of distribution, rate of clearance in tissue, the in vivo consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of RNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced. These factors differ significantly based on the vector used and the protein being produced (Goodman & Gilman's The Pharmacological basis of Therapeutics, McGraw-Hill, New York, NY. pp 77-101). While progress has been made

in recent years for *in vivo* gene transfer, vector targeting *in vivo* to be desired organs continued to be unpredictable and inefficient.

Given this lack of reasonable predictability in Applicant's specification and the art, the Artisan would require a large amount of information from Applicant's examples to provide the guidance to provide reasonable predictability.

Applicant's examples only describe that 15-Lipoxygenase is expressed in eye. Specifically, Example 1 demonstrates that RP-HPLC analyses of conjunctiva samples showing moderate activity in seven out of 21 samples. The specification discloses four samples that were positive for 15- LO activity for RT-PCR analyses. The results showed only one out of four positive for 15-LO-1 and 1 sample positive for both iso-enzyme (see pages 13-14). It is emphasized that neither art nor instant specification explicitly teach that lack of 15-lipoxygenase-1, -2 in postmenopausal patients result in dry eye condition. The specification on page 6, lines 6-7 states, "... present invention stems from the discovery that the ocular surface epithelium of postmenopausal women may lack 15-lipoxygenase (15-LO) (pp 6, line 7)" suggesting it was just a hypothesis. The art of record only implies potential benefit of supplementing 15-lipoxygenase for the treatment of dry eye condition, however, such an implied statement does not provide specific guidance to practice an unpredictable invention. It is also unclear from the specification whether the example disclosed in the specification uses tissues derived from *ex-vivo* or *in vivo* experiment. In addition, Applicants do not provide any specifics on type of vector or method of delivering or route used to express transgene in the subject exemplified in the specification (see page 14). In addition, it is not enough to

reasonably predict that the transgene can be expressed using any vectors delivered via any route at reasonable level for appropriate time duration in appropriate cells of eye for the treatment of dry eye conditions in human or any subject. It is also not apparent how the claimed vectors or other delivery vehicle would be effective in any postmenopausal patients. Artisan could not predict, in the absence of proof to the contrary, that such a method would be efficacious in therapeutic treatment. The specification fails to provide an enabling disclosure for the claimed invention because the specification fails to provide sufficient guidance as to (1) how an artisan of skill would have practiced the claimed method in any subject or a postmenopausal patient (ii) the claimed method would have resulted in expression of 15-lipoxygenase-1,-2 in amount sufficient to treat the dry eye conditions by administering transgenes via any route in "postmenopausal patient". An artisan would have to carry out extensive experimentation to make and use the invention, and such experimentation would have been undue because of the art of gene therapy and gene delivery *in vivo* is unpredictable and specification fails to provide any guidance as to how the claimed method would have been practiced.

Claims 1-3, 5-8 and 14-17 are directed to a method for treating dry eye condition by administering a composition comprising SEQ ID NO: 1 or 3 under condition such that it is expressed. Subsequent claim limit the method to include administering the composition in the topical or ointment form. The specification contemplates contacting an ocular cell with exogenous nucleic acid under conditions that allow the ocular cell to take up the exogenous nucleic acid into the ocular cell and express it. It is noted that specification only teaches that this expression may be accomplished by means familiar

to the skilled artisan or methods described in U.S. Patent No. 6, 204, 251 (see page 7, paragraph 3). The specification provides no guidance in terms of whether transgene delivered by methods known in the art would result in expression of 15-lipoxugenase-1 and –2 for adequate time at a level sufficient to elicit pharmacological response. This is particularly important since prior to instant invention, the state of the prior art effectively summarized by the references of Verma and Somia (1997) Nature 389:239-242 and Pfeifer and Verma (2001) Annual Review of Genomics and Human Genetics.2: 177-211 describes progress made in developing new vectors and also suggest vector targeting *in vivo* to be unpredictable and inefficient. Verma et al., reviews various vectors known in the art for use in gene therapy and problems associated with each implying that at the time of claimed invention resolution to vector targeting had not been achieved in the art (Verma et al., 1997; Pfeifer et al., 2001; entire article; IDS). They highlight some advantages of using retroviral and adeno-associated viral vector in gene therapy but also acknowledge a greater level of skepticism in using these vectors in human (Pfeifer et al., 2001; abstract). It is noted by the authors that more efficient and safe vectors are required to deliver gene to the target cell for therapeutic effective level of gene expression (Pfeifer and Verma 2001, Annual Review of Genomics and Human Genetics.2: 177-211, pp 201).

Next, the claims (9-13 and 18-22) recite vectors and plasmid for delivering transgene in ocular cells. The specification teaches that the cornea is readily accessible to gene therapy by injection of naked plasmid DNA into the cornea (see page 7, para. 2). Upon further review, it is noted that Stechschulte, et al. (2001) Investigative

Ophthalmology & Visual Science: 42(9): 1975-1979; IDS), teach efficacy and safety of naked plasmid gene therapy to the corneal stroma and epithelium of mice. However, authors also conclude that how broadly these technique would be applied could be determined only by ongoing work in the art (pp 1978, last paragraph). Thus, while art of record teaches administration of naked DNA to cornea in ocular disease of mice, these findings cannot be extrapolated for a very specific treatment of dry eye condition prevalent in postmenopausal patient. The specification merely provides a general description that is not sufficient to provide enabling support because claimed therapy method cannot be actually reduced to practice until the skilled artisan is provided by sufficient guidance to how much and how long the transgene expression would be required to attain therapeutic response in postmenopausal patients. These methods would have required undue experimentation because neither the specification nor the art of record teaches specific guidance for treating dry eye condition by over expressing 15-lopoxygenase-1, -2 in postmenopausal patients.

Next, Behrens, et al. (2002) Investigative Ophthalmology & Visual Science: 43(4): 968-977, IDS, teaches *in vivo* efficacy and safety of ophthalmic topical treatment of a retroviral vector bearing an antiproliferative dominant negative mutant cyclin G1 (dnG1) construct in corneal haze after phototherapeutic keratectomy (PTK) in rabbit. In addition, Kamata et al., (Mol Ther. 2001, 4(4): 307-312, IDS) teach adenovirus-mediated transduction efficiency in mouse eyes using an adenoviral vector expressing *E. coli* β-galactosidase. It is emphasized that they failed to transfer gene onto the cornea by administering drops of a solution containing adenovirus AxCALacZ. However,

direct injection of adenovirus expressing AxCALacZ into the anterior chamber resulted in Lac Z expression in the inner layer of cornea (pp 308, 3rd paragraph).

Martin, et al. (2002) Methods: 267-275, IDS, evinces an optimistic outlook for the treatment of ocular disorder using adneo-associated viral vector (AAVV), but also acknowledges that the art is not yet generally enabling for humans (pp 268 3rd paragraph). It is noted that Martin et al (Methods 2002: 267-275, IDS) emphasize that efficiency of transfection of specific cell types of eye are dependent on a number of variables including the site of injection, the AAV serotype and titer and the amount of DNA (pp 268-269). The specification does not provide any specific guidance to address these issues.

Furthermore, in the instant case, the results of Cuthbertson ('251) or Stechschulte, or Behrens or Kamata or Martin cannot be predictive of treating deficiency of 15-lipoxygenase in treating dry eye condition of postmenopausal patient because above described methods and compositions are used in different animal model for different diseases and therefore cannot be extrapolated to treating a very specific dry eye condition prevalent in specific population of postmenopausal patient. This fact is supported by the fact that no appropriate animal model exists for dry eye condition. In fact, recently Barabino et al., (Investigative Ophthalmology & Visual Science. 2004,45(6): 1641-1646, IDS) describe, "all the existing animal models of dry eye mimic different pathogenic mechanisms of Dry eye syndrome, or keratoconjunctivitis sicca (KCS) and at the moment none of them seems to mirror precisely the complexity and chronicity of this frequent and debilitating condition" (pp1645; Conclusion). This clearly

establishes the unpredictability of the animal models currently being used for evaluating therapeutics effective against dry eye. Therefore, methods of expressing transgene in any other disease model cannot be directly extrapolated to treatment of dry eye conditions in humans. The specification also does not provide any guidance as to how studies in animal model of different disease can be extrapolated to the treatment of dry eye condition in any subject including humans. Furthermore, It is also noted that, the specification does not teach whether viral vectors or plasmid can be used effectively in administering transgene either via any route in postmenopausal patients. In addition, prior art at the time of filing of this application as described before did not provide any convincing guidance in this regard either.

The scope of invention of claims 1-2, 4-22 encompasses administering the composition using non-viral and viral vector via any or all route of administration (i.e oral, intranasal, intramuscular, intravenous, subcutaneous etc). It has been difficult to predict the efficacy and outcome of transduced therapeutic genes because factors govern the expression and/or therapeutic potential of transduced gene *in vivo* (supra Goodman & Gilman's The Pharmacological basis of Therapeutics, McGraw-Hill, New York, NY. pp 77-101). The transduction of target cells represent the first critical step in any gene based therapy, which not only depends upon the type of target cells but also on the choice and/or characteristics of delivery vectors. In addition, besides the limitations in gene transfer the problem to selectively target cell s *in vivo* is still one of the most difficult obstacles to overcome. For example, upon systemic administration the viral and non-viral particle may bind to many cells they encounter *in vivo* and therefore

would be diluted before reaching their targets. In the instant case, specification does not provide any specific guidance and solely relies on prophetic teachings of prior art that are primarily directed to different methods and treatment different disease. It is noted that neither prior art nor specification provided any guidance whether any or all routes of administration would result in generation of sustained expression of 15-LO-1, -2 at minimum effective level to elicit any pharmacological response in any subject particularly since prior art also disclosed non availability of good animal model to study dry eye conditions.

In reviewing the above-discussed problem, it is evident that the artisan would require, making and/or using a new invention in the field. A showing that enough of 15-lipoxygenase-1, -2 reaches the target cell, enough nucleic acid is incorporated into ocular cells, that such nucleic acid is properly incorporated into such cells as DNA, enough mRNA is produced therefrom, and enough protein is produced and 15-lipoxygenase-1, -2 have an effect on the ocular cells and such effect is enough of an effect for a long enough period of time. Alternatively, direct example of such effect of 15-lipoxygenase-1, -2 would overcome this showing specifically for 15-lipoxygenase-1, -2 if these transgenes are included in the vector they must have met the requirement above.

The cited arts clearly indicate an unpredictable status of the gene therapy art pertaining to treatment of dry eye condition. Although, specific vectors, promoters, genes, and route of administration might be or may have been effective for treatment of specific disease providing specific therapeutic effect. Gene therapy as a broad-based

art is clearly unpredictable in terms of achieving levels and duration of expression of a gene of interest, which results in a therapeutic effect.

In conclusion, in view of breadth of the claims and absence of a strong showing by Applicant, in the way of specific guidance and direction, and/or working examples demonstrating the same, such invention as claimed by Applicant is not enabled. The specification and prior art do not teach a method of *in vivo* delivery of a gene such that it is expressed at therapeutic effective level for desired duration in the eye of any subject or postmenopausal patient suffering from dry eye condition. An artisan of skill would have required undue experimentation to develop/design a suitable vector and practice the method as claimed because the art of gene therapy, vector design and *in vivo* delivery and treatment of dry eye condition was unpredictable at the time of filing of this application as supported by the observations in the art record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 6-8 and 15-17 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because the method does not recite a positive step linking the preamble to the steps of the claimed method. The claim merely recites

administering the composition to a patient suffering from dry eye condition without any active, positive step delineating how claimed method will actually be practiced resulting in the treatment of dry eye. Claims 2-3 depend on claim 1.

Claims 6-8 and 15-16 are improperly dependent claims because they depend on themselves. Claim 17 depends on claim 7. Appropriate correction is required.

Claims 8 and 17 recite the limitation "exogenous nucleic acid" in the claim. There is insufficient antecedent basis for this limitation in the claim.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 5-22 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 5-22 of copending Application No. 10/688,676. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. It is noted that the conflicting claims are identical and are not patentably distinct from each other because both sets claim a method of treating dry eye in a post menopausal patient by delivering the same composition using same method steps. In particular, claim 5 of the '676 is directed to a method of treating dry eye in a

postmenopausal patient by incorporating nucleic acid into an in situ ocular cell under conditions permissive for the uptake of said nucleic acid encoding a protein having the sequence set forth in SEQ ID NO: 2, whereby said nucleic acid is expressed and disease is treated. It is noted that instant claims also recite same method steps for treating dry eye condition. Likewise, subsequent claim limits the nucleic acid sequence comprises to include sequence set forth in SEQ ID NO: 1. Claim 7 limits the method to include cell that is a conjunctival or corneal epithelial cell. Claim 8 limits the method to include cell that is debrided prior to introducing said exogenous nucleic acid. Claims 9-10 limit the nucleic acid to include a viral vector and plasmid. Subsequent claim limit the nucleic acid to include a retrovirus, an adenovirus or an adeno-associated virus. Claim 14 is directed to a method of treating dry eye in a postmenopausal patient by incorporating nucleic acid into an in situ ocular cell under conditions permissive for the uptake of nucleic acid, wherein nucleic acid encoding a protein having the sequence set forth in SEQ ID NO:4, whereby nucleic acid is expressed and the disease is treated. Claim 15 limits the nucleic acid sequence to include sequence set forth in SEQ ID NO:3. Claims 16-17 limit the cell that is a conjunctival or corneal epithelial cell and is debrided prior to introducing exogenous nucleic acid. Claims 18-22 limit method to include nucleic acid that is in a viral vector or a plasmid, a retrovirus, an adenovirus or in an adeno-associated virus vector. It is noted that the instant claims 1-22 are identical to claims 5-22 of '676 application.

Conclusion

No Claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anoop Singh whose telephone number is (571) 272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272- 4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anoop Singh, Ph.D.
Examiner, AU 1632

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER